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**Hierarchical molecular events driven by oocyte-specific factors lead to rapid and extensive reprogramming.**

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**Public Summary:**

In this work we identified how key molecules stored in an oocyte reprogram somatic nuclei following nuclear transfer.

**Scientific Abstract:**

Nuclear transfer to oocytes is an efficient way to transcriptionally reprogram somatic nuclei, but its mechanisms remain unclear. Here, we identify a sequence of molecular events that leads to rapid transcriptional reprogramming of somatic nuclei after transplantation to *Xenopus* oocytes. RNA-seq analyses reveal that reprogramming by oocytes results in a selective switch in transcription toward an oocyte rather than pluripotent type, without requiring new protein synthesis. Time-course analyses at the single-nucleus level show that transcriptional reprogramming is induced in most transplanted nuclei in a highly hierarchical manner. We demonstrate that an extensive exchange of somatic- for oocyte-specific factors mediates reprogramming and leads to robust oocyte RNA polymerase II binding and phosphorylation on transplanted chromatin. Moreover, genome-wide binding of oocyte-specific linker histone B4 supports its role in transcriptional reprogramming. Thus, our study reveals the rapid, abundant, and stepwise loading of oocyte-specific factors onto somatic chromatin as important determinants for successful reprogramming.

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